ABSTRACT

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Title of rigorous thesis: Effect of flubendazole on proliferation of colorectal carcinoma cell lines *in vitro*

Flubendazole is widely used anthelmintic drug belonging to benzimidazole group. The molecular mechanism of action of flubendazole is based on specific binding to tubulin, which results in disruption of microtubule structure and function and in the interference with the microtubule-mediated transport of secretory vesicles in absorptive tissues of helminths. The microtubule-disrupting properties of benzimidazole derivatives raised recently interest in these compounds as possible anti-cancer agents. Because of available studies and pharmacological statements, it is supposed considerable concentrations of flubendazole in intestinal cells after p.o. administration could be reached, we performed this study to investigate the antiproliferative potential of flubendazole in a panel of intestinal cancer cell lines.

The colorectal carcinoma cell lines SW480, SW620 and one cell line NCM460 isolated from normal colon mucosa were treated with different concentrations of flubendazole (0.1 – 10 μM) for 24, 48 and 72 hours. Cell viability was assayed using NRU test and WST-1 test. The effect of flubendazole on the cell cycle distribution of SW480 was analysed with flow cytometry. Other specific methods such as fluorescent staining of tubulin and nuclei, measurement of caspase 3 activity and β-galactosidase staining, were used to investigate the mechanism of action of flubendazole on the cells. Flubendazol induced accumulation of cells in G2/M phases of the cell cycle and significantly inhibited cell proliferation in concentration-dependent and time-dependent manner in comparison to the control samples.

In conclusion, anthelmintic benzimidazole drug flubendazole shows significant cytostatic effect in human intestinal cancer cell lines.